PATENT COOPERATION TREA

From the INTERNATIONAL BUREAU

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NOTIFICATION CONCERNING TRANSMITTAL OF COPY OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (CHAPTER I OF THE PATENT COOPERATION TREATY)
(PCT Rule 44bis.1(c))

To:

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Date of mailing *(day/month/year)*	
14 September 2006 (14.09.2006)	
Applicant's or agent's file reference A0852.70000	**IMPORTANT NOTICE**
International application No. PCT/US2005/007519	International filing date *(day/month/year)* 03 March 2005 (03.03.2005)
Priority date *(day/month/year)* 03 March 2004 (03.03.2004)	
Applicant ADRA, Chaker, N.	

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference A0852.70000	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2005/007519	International filing date *(day/month/year)* 03 March 2005 (03.03.2005)	Priority date *(day/month/year)* 03 March 2004 (03.03.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant ADRA, Chaker, N.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 05 September 2006 (05.09.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Simin Baharlou e-mail: pt09@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

15/9

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2005/007519	03.03.2005	03.03.2004

International Patent Classification (IPC) or both national classification and IPC
C12Q1/68, G01N33/53

Applicant
ADRA, Chaker N.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 61-71

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 61-71 are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☒ the claims, or said claims Nos. 61-71 are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 61-69 (in part)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	28-48
	No:	Claims	1-27,49-60
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-60
Industrial applicability (IA)	Yes:	Claims	1-60
	No:	Claims	

2. Citations and explanations

see **separate sheet**

Re Item III.

1 **Clarity, Support and Disclosure** (Art. 5 and 6 PCT)

1.1 A search report has been established based on the alleged effects of the compound/compositions of claims 61-69.

1.2 The application does not meet the requirements of Article 6 PCT, because claims 61-71 are not clear and not supported by the description. The matter for which protection is sought is not clearly defined. The claims relate to compounds and compositions that are defined by reference to a desirable characteristic or property, namely that they interact with a marker in an amount sufficient to treat a disease or that they alter a physiological property of a cell. The claims cover all compounds and compositions having this characteristic or property, whereas the application does not provide support within the meaning of Article 6 PCT or disclosure within the meaning of Article 5 PCT for any of said compounds or compositions. This leads also to a lack of clarity and support of claims 62 and 67, since it is unclear how the modulation of the activity or expression of a marker shall be performed. Thus claims 61-71 lack support and clarity (Article 6 PCT) and the application lacks support (Article 5 PCT). Consequently no opinion regarding the novelty, inventive step and industrial applicability of the subject matter of said claims has been formulated.

Re Item V.

2 Reference is made to the following documents:

D1: US 2004/038252 A1 (SUGITA YUJI ET AL) 26 February 2004

D2: WO 99/10536 A (YALE UNIVERSITY; YERRAMILLI, SUBRAHMANYAM, V; PRASHAR, YATINDRA; NEWBU) 4 March 1999

D3: WO 02/33122 A (GENOX RESEARCH, INC; JAPAN AS REPRESENTED BY GENERAL DIRECTOR OF NATIO) 25 April 2002

D4: US 2003/069196 A1 (LEVINSON DOUGLAS ADAM ET AL) 10 April 2003

D5: WO 97/39148 A (CEDARS-SINAI MEDICAL CENTER) 23 October 1997

3 **Novelty and Inventive Step** (Art. 33(2) and 33(3) PCT)

3.1 D1 discloses a method for diagnosing a non-neutrophil, granulocyte disorder (atopic dermatitis, par. 11-17), by comparing the expression level of a granulocyte selective marker (a gene expressed in eosinophils) of a subject with a reference (healthy person, claim 1) in order to diagnose a disorder. D1 also discloses the use of the marker gene in order to identify a compound that alters the expression of the gene (par. 23-37). D1 discloses that the expression of the marker gene is indicative of a regression (par. 12-13). D1 thus discloses all the technical features of claims 1,14, and 49 in combination.

3.2 D2 discloses a method for diagnosing a granulocyte disorder (sterile inflammatory disease, ex. 10), by comparing the expression level of granulocyte selective markers (neutrophil mRNA species, ex. 10) of a subject with a reference (patient) in order to diagnose a disorder. D2 also discloses a method to identify a compound that alters the expression of the granulocyte marker in order to identify a therapeutic agent (ex. 5 and 6). D2 thus discloses all the technical features of claims 1 and 49 in combination.

3.3 Consequently in the light of D1 and D2 independent claims 1, 14 and 49 are not novel in the sense of Art. 33(2) PCT.

3.4 Due to the fact that D1 already discloses a marker gene whose expression is used in order to screen for a candidate compound for a therapeutic agent (par. 42) and as well discloses a marker gene whose expression depends on the stage of the disease (par. 13-14), the use of this marker to monitor the response to a treatment and to determine regression of a disorder are regarded as normal modifications of the method of D1 that the person skilled in the art would perform without an inventive step. Consequently the subject matter of the independent claims 28, 35 and 42 cannot be regarded as being inventive.

3.5 Thus for the reasoning given above the independent claims 1, 14, 28, 35, 42 and 49

do not fulfil the requirements of inventive step of Art. 33(3) PCT.

3.6 In the light of D1 and D2 dependent claims 2-13, 15-27, 29-34, 36-41 and 43-48 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.

3.7 Additionally in the light of D3 (abstract), D4 (par. 344), and D5 (example 1) the subject matter of claims 1-60 do not meet the requirements of the PCT in respect of inventive step.

3.8 Consequently claims 1-60 do not fulfil the requirements of novelty and/or inventive step of Art. 33(2) and 33(3) PCT.

4 Irrespective of points raised above claims 61-69 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).